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Chlorhexidine gel to prevent alveolar osteitis following mandibular third molar extractions

Abstracted from

Amare Teshome.

The efficacy of chlorhexidine gel in the prevention of alveolar osteitis after mandibular third molar extraction: a systematic review and meta-analysis. *BMC Oral Health* 2017;17:82.

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Question: Does chlorhexidine (CHX) gel placed in the extraction socket postoperatively reduce the incidence of alveolar osteitis (AO) after a mandibular third molar extraction?

Data sources

Medline/PubMed, Cochrane central, Scopus and Google scholar.

Study selection

Randomised controlled trials (RCTs) published in English language between January 2010 and December 2015 were identified by two reviewers. Unpublished studies were not considered.

Data extraction and synthesis

Standard Cochrane Collaboration assessment tools were used to carry out a risk of bias assessment. The following data was collected from the articles; sample size, country, mean age of participants, diagnosis of alveolar osteitis (AO), type of intervention and outcomes. Heterogeneity (I^2) was calculated to determine the statistical model to be used for meta-analysis.

Results

Ten randomised control trials (RCTs) were included, with 862 participants. Eight studies used 0.2% chlorhexidine (CHX) gel in the experimental group; 1% CHX gel in one study, and one study the concentration was not specified. Two studies used adjunctive antibiotics, and one study gave 400mg Ibuprofen to all participants.

Six of the RCTs were at low risk of bias, three studies with possible selection and/or performance bias, and one study with no information on bias. Heterogeneity was low level ($I^2 = 40\%$) and a funnel plot presented a low level of publication bias.

The included RCTs used Blum's criteria for diagnosis of AO. Six of the RCTs were conducted double-blinded. The risk ratio (RR) was calculated for each RCT and also for the pooled effect. The overall pooled effect of CHX gel placed in the extraction socket following mandibular 3rd molar removal was calculated to have prevented 57% of AO instances (RR = 0.43, 95%CI: 0.32, 0.58; $p < 0.00001$). Subgroup analysis of the effect of CHX gel in participants who smoked/used the oral contraceptive pill (OCP) was calculated to have prevented 40% of AO (RR = 0.60, 95%CI: 0.41, 0.87; $p = 0.007$). In the studies that used a split-mouth design, CHX gel prevented 71% of AO incidence (RR = 0.29, 95%CI: 0.16, 0.50; $p < 0.00001$).

Conclusions

This meta-analysis and systematic review concluded "clinically significant evidence that CHX gel application in the extraction socket of mandibular 3rd molar has reduced the incidence of alveolar osteitis".

Commentary

Alveolar osteitis (AO) or dry socket, is a common post-operative complication of dental extractions and is often extremely painful. It can be classified using Blum's criteria¹; "postoperative pain in and around the extraction site, which increases in severity at any time between one and three days after the extraction, accompanied by a partially or totally disintegrated blood clot within the alveolar socket, with or without halitosis". AO is associated with significant morbidity for patients, as well as cost implications for patients and dentists. It occurs more frequently after mandibular extractions due to a more restrictive blood supply compared to maxillary teeth. The 2012 Cochrane review² reported the incidence of AO to be between 1% and 5% following routine extractions but greater than 30% for surgical extractions of third molars. They found a benefit from both CHX rinsing (0.12% and 0.2), with 42% AO being prevented, and for CHX gel (0.2%) being placed into the

socket after extraction, with approximately 58% AO prevented. However, the number of patients who needed to be treated (NNT) to prevent one patient experiencing AO was significantly influenced by the background prevalence. So, when the background prevalence of AO was 1%, the NNT was 173 (95% CI 127 to 770), against a 5% background prevalence the NNT was 35 (95% CI 25 to 154) and for 30% prevalence, the NNT was 6 (95% CI 5 to 26).

Other systematic reviews have also shown positive results for CHX in preventing AO^{3,4}, but there is little information to inform the most clinically effective treatment considering costs and potential harms/side effects. Anaphylaxis as a result of CHX has been a topic of great discussion in recent years, and dental practitioners have been advised to be aware of the potential for hypersensitivity reactions, particularly when considering use in the “open wound” of an extraction socket⁵. There is a need for evidence to help inform decisions about whether the therapeutic use of CHX would outweigh its drawbacks in the prevention of AO; whether the benefits are more significant in specific groups of patients and what the threshold background rate would need to be for benefit to outweigh harm and be cost-effective.

The current systematic review by Teshome adds to the evidence supporting the use of CHX gel in the prevention of AO with the meta-analysis risk ratio (RR) demonstrating benefit. However, there are some details that those considering integrating the results into their clinical practice should consider carefully. The systematic review was not registered, nor was a protocol published; this could have potentially introduced bias into the systematic review process. The methods of this systematic review imply that the included studies should compare CHX gel to a placebo gel. However, six of the included studies compared CHX gel to controls other than placebo gel and therefore did not meet this inclusion criteria. This poses the question as to why these studies were included.

This review reports that the overall efficacy of CHX gel would prevent 57% of AO, expressed as RR this was 0.43. The author did not calculate the NNT and we were unable to convert the results to a NNT because we are not given the background prevalence rates across the studies (and these may have varied because the control groups differed), this lack of homogeneity makes the interpretation of a NNT potentially meaningless. Being able to express the result as a NNT would have helped clarify the effectiveness of CHX in clinical and economic contexts.

There are a few other methodological drawbacks that should be kept in mind when interpreting the results of this review. Firstly, whilst this systematic review included 10 RCTs in the meta-analysis, only nine were presented in the results of the risk of bias assessment and whilst risk of bias was clearly assessed, there was no specific information on the certainty of the evidence of the strength of the evidence (the GRADE approach). Secondly, the number of studies identified in the systematic review may have been reduced by including only papers published in English, and within a recent six-year period (2010-2015). For example, looking at the 2012 Cochrane review, this included two studies from 2006 which investigated 0.2% CHX gel in preventing AO, these were not included in the current study due to the restricted time period (January 2010 to December 2015). Inclusion of these studies may not have altered the overall conclusion, but could have influenced the size of the overall benefit-effect identified. This review stated that the included studies did not report any adverse effects of CHX but there was very little information/discussion regarding this issue and it was not clear if/how the included studies specifically looked for adverse effects. A further point is that the references for two of the detailed RCTs did not seem to match the description in the main body of the review.

This review addressed an important issue; AO is a common problem following dental extractions and even more so in certain high risk groups. This review did include a sub-group analysis, showing benefits of CHX gel even in patients who smoke or take the oral contraceptive pill, however these two risk factors were not presented separately. It would be beneficial for future studies to individually explore risk factors. This would support the practitioner in targeting treatment towards patient groups likely to obtain most benefit from CHX as an adjunct following extraction of third molars, and reducing the use of CHX in low risk groups and possible adverse events. Despite the possible inaccuracies in how this systematic review was reported, it does appear to provide some evidence to support the use of CHX gel in the prevention of AO. Any benefit of CHX in preventing AO needs to be weighed up carefully against the potential risk of hypersensitivity reactions and the background AO rate. Further consideration needs to be given to which patient groups would benefit most and the threshold rate for likely benefit to be achieved over possible harm.

Practice points

- This systematic review states that it provides evidence to support the use of CHX gel in the prevention of AO. However, due to the limitations discussed above, readers should interpret the results with caution.
- Any benefit of CHX in preventing AO should be weighed up carefully against the potential risk of hypersensitivity reactions and the background AO rate. Further research is required to determine which patient groups would most benefit from this intervention and what the threshold background rate is for likely benefit.

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